REMARKS

The Examiner is thanked for the due consideration given the application. A Declaration and CV are appended to this paper.

Upon entry of this amendment claims 28, 29 and 31-54 are pending in the application. By this amendment claim 30 is canceled and its subject matter is generally incorporated into claim 1. Claims 49-54 have been withdrawn.

No new matter is believed to be added to the application by this amendment.

Entry of this amendment under 37 CFR §1.116 is respectfully requested because it cancels a claim and places the application in condition for allowance.

Rejections Under 35 USC §103(a)

Claims 28-33 and 36-48 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over JANSEN (US 2004/0071716; filed 2/20/2002) in view of WESTESEN (US 6,207,178; issued 3/27/2001).

Claims 28, 34 and 35 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over JANSEN in view of WESTESEN and RABUSSIER (US 3,258,326; issued 6/28/1966).

These rejections are respectfully traversed.

The aim of the present invention is to obtain~~s~~ systems for the administration of active principles, which allow a high concentration of active principle and show a high colloidal

stability even at high concentration, thereby avoiding all problems linked to particle aggregation.

The administration systems of the present invention are in the form of a composition comprising monodisperse solid lipid particles having a size of 1 to 6 micrometers (see independent claim 28).

These compositions may be produced by a process where the lipid phase containing the active principle is emulsified with an aqueous phase in the presence of a stabilizer, and the resulting emulsion is then subjected to a shear.

It is respectfully submitted that such a composition is patentable over the cited prior art.

As recognized by the Office Action, JANSEN discloses compositions which differ from those presently claimed in particular in that they do not comprise a crystallizable lipid.

On the other hand, WESTESEN discloses compositions which include a crystallizable lipid, but where the particles have a size outside the claimed range of 1 to 6 micrometers and are not monodispersed. Indeed, WESTESEN discloses solid particles which have a size ***under 500 nm*** most often between 50 and 300 nm (see column 12, line 17).

While it is true that, as pointed out by the Office Action, JANSEN and WESTESEN both teach stable compositions, it is submitted that this fact alone would not have motivated the skilled person to achieve the present invention.

Indeed, the stability of a composition may be the result of different technical teachings, in particular if the compositions are of a different nature.

In that respect, WESTESEN teaches that stable compositions require the presence of highly mobile stabilizing agents in the dispersion medium, such as bile salts in combination with glycerol (see column 12, lines 30-45).

In contrast, JANSEN teaches that stable emulsions may be obtained ***by adding a polymeric emulsifier*** which is a block copolymer having a general formula A-COO-B-OOC-A (see [0012]~~)~~~~.~~.

WESTESEN and JANSEN thus teach different routes to obtain a stable composition.

This is not surprising because the disclosed compositions also differ: on one hand, a monodisperse ***emulsion*** and, on the other hand, a finely dispersed ***suspension***~~.~~.

The teachings of JANSEN and WESTESEN thus differ~~s~~ by far more than just the lipid component of the composition.

In contrast, the present invention sets forth yet another route to obtain a stable composition, since the stabilizer used to prepare the claimed composition is a compound bearing two fatty acid chains and one polyethylene glycol chain.

It is thus submitted that the skilled person would have no reason to include crystallizable lipids in~~to~~ the composition taught by JANSEN, because the skilled person could not expect that this would necessarily lead to a stable composition.

In this respect, WESTESEN clearly points out that suspensions of solid lipids are not equivalent to lipid emulsions, that the physicochemical properties of lipid suspensions differ substantially from that of lipid emulsions and that lipid suspensions cannot be prepared and treated analogously to lipid emulsions (column 13, line 61 to column 14, line 1).

Further, the skilled person could not expect the monodisperse solid lipid particles in the composition obtained to have a size of 1 to 6 micrometers, as now claimed.

Therefore, the skilled person facing the problem of providing a composition stable even in high concentration of lipid particles, that is up to and exceeding 5%, it is not obvious to turn to WESTESEN in regards to compositions according to JANSEN.

At page 13 the Office Action asserts "that no evidence has been put forth to support the assertion that any differences in the two types of suspensions would render the combination of JANSEN and WESTESEN inoperable."

Herewith enclosed is a Declaration under Rule 132 by one of the inventors, Jérôme Bibette, along with his CV.

The Declaration confirms in particular that:

- The skilled person would not have been motivated to add crystallisable lipids according to WESTESEN into the emulsions according to reference JANSEN because this would have increase the viscosity of the compositions.

- Even if the skilled person had applied this teaching, this would not have led to the compositions as claimed because the equipment proposed in JANSEN has a high rotation speed which is not suitable for obtaining compositions comprising monodisperse crystallisable lipid particles, which requires application of shear.

- The homogeneity of size distribution of monodisperse particles is an important factor in the context of oral administration as they influence the release rate of the active principle, the interactions with the gastrointestinal mucosa and the degradation by the digestive enzymes and the passage through the intestinal epithelium and also in the context of subcutaneous administration since it influences the release rate of the active principle, the degradation rate of the particles and their subcutaneous residence time and their interaction with the immune system.

As a result, the Declaration demonstrates that combining the teachings of JANSEN and WESTESEN would not produce the present invention, but rather result in an inoperable technology.

If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

RABUSSIER fails to address the deficiencies of JANSEN and WESTESEN set forth above and in the Declaration.

One or ordinary skill and creativity would thus not produced a claimed embodiment of the present invention from a knowledge of the applied art. A *prima facie* case of unpatentability has thus not been made, especially in light of the Declaration.

These rejections are believed to be overcome, and withdrawal thereof is respectfully requested.

Foreign Priority Claim

Since JANSEN's filing date of 2/20/2002 appears to predate the earliest date of 10/13/2003 associated with the present invention, it is believed that there are no issues pertaining to priority that need to be further explored at this point in the prosecution of the application.

Conclusion

The issuance of a Notice of Allowability is respectfully solicited.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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APPENDIX:

- Declaration and CV